Complete Summary

GUIDELINE TITLE

Depression.

BIBLIOGRAPHIC SOURCE(S)

University of Michigan Health System. Depression. Ann Arbor (MI): University of Michigan Health System; 2005 Oct. 20 p. [3 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: University of Michigan Health System. Depression. Ann Arbor (MI): University of Michigan Health System; 2004 May. 21 p.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- On May 12, 2006, GlaxoSmithKline (GSK) and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of changes to the Clinical Worsening and Suicide Risk subsection of the WARNINGS section in the prescribing Information for Paxil and Paxil CR. These labeling changes relate to adult patients, particularly those who are younger adults.

  A recent meta-analysis conducted of suicidal behavior and ideation in placebo-controlled clinical trials of paroxetine in adult patients with psychiatric disorders including Major Depressive Disorder (MDD), other depression and non-depression disorders. Results of this analysis showed a higher frequency of suicidal behavior in young adults treated with paroxetine compared with placebo. Further, in the analysis of adults with MDD (all ages), the frequency of suicidal behavior was higher in patients treated with paroxetine compared with placebo. This difference was statistically significant; however, as the absolute number and incidence of events are small, these data should be interpreted with caution. All of the reported events of suicidal behavior in the adult patients with MDD were non-fatal suicide attempts, and the majority of these attempts (8 of 11) were in younger adults aged 18-30. These MDD data suggest that the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24.

It is important that all patients, especially young adults and those who are improving, receive careful monitoring during paroxetine therapy regardless of the condition being treated. See the FDA Web site for more information.

- On December 8, 2005, the U.S. Food and Drug Administration (FDA) has determined that exposure to paroxetine in the first trimester of pregnancy may increase the risk for congenital malformations, particularly cardiac malformations. At the FDA's request, the manufacturer has changed paroxetine's pregnancy category from C to D and added new data and recommendations to the WARNINGS section of paroxetine's prescribing information. FDA is awaiting the final results of the recent studies and accruing additional data related to the use of paroxetine in pregnancy in order to better characterize the risk for congenital malformations associated with paroxetine. Physicians who are caring for women receiving paroxetine should alert them to the potential risk to the fetus if they plan to become pregnant or are currently in their first trimester of pregnancy. Discontinuing paroxetine therapy should be considered for these patients. Women who are pregnant, or planning a pregnancy, and currently taking paroxetine should consult with their physician about whether to continue taking it. Women should not stop the drug without discussing the best way to do that with their physician. See the FDA Web site for more information.
- On October 17, 2005, Eli Lilly and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of revision to the PRECAUTIONS/Hepatotoxicity section of the prescribing information for Cymbalta (duloxetine hydrochloride), indicated for treatment of major depressive disorder and diabetic peripheral neuropathic pain. Postmarketing reports of hepatic injury (including hepatitis and cholestatic jaundice) suggest that patients with preexisting liver disease who take duloxetine may have an increased risk for further liver damage. The new labeling extends the Precaution against using Cymbalta in patients with substantial alcohol use to include those patients with chronic liver disease. It is recommended that Cymbalta not be administered to patients with any hepatic insufficiency. See the FDA Web site for more information.
- On July 1, 2005, in response to recent scientific publications that report the possibility of increased risk of suicidal behavior in adults treated with antidepressants, the U.S. Food and Drug Administration (FDA) issued a Public Health Advisory to update patients and healthcare providers with the latest information on this subject. Even before the publication of these recent reports, FDA had already begun the process of reviewing available data to determine whether there is an increased risk of suicidal behavior in adults taking antidepressants. The Agency has asked manufacturers to provide information from their trials using an approach similar to that used in the evaluation of the risk of suicidal behavior in the pediatric population taking antidepressants. This effort will involve hundreds of clinical trials and may take more than a year to complete. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Depression including:

- Major depressive disorder
- Minor depression
- Dysthymia
- Seasonal affective disorder
- Mood disorders associated with a general medical condition

GUIDELINE CATEGORY

Diagnosis
Management
Screening
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Psychiatry
Psychology

INTENDED USERS

Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

- To improve the early recognition and treatment of depression in the primary care setting
- To familiarize clinicians with appropriate treatment options, drug side effects, and interactions
- To improve patient's understanding of depression as a treatable illness
- To identify when referral is indicated

TARGET POPULATION

Adults with depressive disorders

INTERVENTIONS AND PRACTICES CONSIDERED

Screening and Diagnosis

1. Patient Health Questionnaire (PHQ-9)
2. History
3. Evaluation
4. Physical examination
5. Laboratory testing

Treatment

1. Supportive care:
    - Patient education
    - Exercise
2. Pharmacotherapy:
    - Selective Serotonin Reuptake Inhibitors (SSRIs)
        - citalopram (Celexa)
        - escitalopram (Lexapro)
        - fluoxetine (Prozac, Sarafem, Prozac Weekly)
        - paroxetine (Paxil, Paxil CR)
        - sertraline (Zoloft)
    - Serotonin-2 Antagonist/Reuptake Inhibitor
        - nefazodone (Serzone)
    - Serotonin/Norepinephrine Reuptake Inhibitor (SNRIs)
        - venlafaxine (Effexor XR)
        - duloxetine (Cymbalta)
    - Serotonin & alpha-2 Receptor Blocker
        - mirtazapine (Remeron)
    - Norepinephrine/Dopamine Reuptake Inhibitor
        - bupropion (Wellbutrin SR, Wellbutrin XL, Wellbutrin IR)

3. Psychotherapy:
    - Any psychotherapy
    - Interpersonal psychotherapy (IPT)
    - Cognitive behavioral psychotherapy (CBT)
    - Marital therapy
4. Treatments for severe or refractory depression:
    - Electroconvulsive therapy, monoamine oxidase inhibitors (MAOIs), lithium, thyroid hormone supplementation, valproic acid, antidepressant augmentation, stimulant medication, referral
5. Controversial Areas (No specific recommendations made)
    - St. John's Wort (hypericum perforatum)
    - Withdrawal syndrome

MAJOR OUTCOMES CONSIDERED

- Mortality rates by suicide
- Depressive symptoms
- Time to respond to pharmacotherapy
- Frequency and severity of relapses
- Outpatient visits and inpatient hospitalization
- Mortality from myocardial infarction
- Direct and indirect costs (including direct patient care, time lost from work, and potential income loss due to suicide) associated with major depressive disorder

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The literature search for this update began with results of the literature search performed in 1997 to develop the initial guideline. The literature search conducted in 2002 for this project was conducted prospectively on Medline using the major keywords of depression, depressive disorders; consensus development conferences, practice guidelines, guidelines, outcomes and process assessment (health care); clinical trials, controlled clinical trials, multicenter studies, randomized controlled trials, cohort studies; adults; English language; and published between 1/1/97 and 9/30/02.

Terms used for specific topic searches within the major key words included epidemiology; national cost of treatment (economics); screening (for depression, bipolar disorder; alcohol abuse); diagnosis; suicide risk assessment; patient education; exercise; serotonin selective reuptake inhibition (citalopram, escitalopram, fluoxetine, paroxetine, sertraline), serotonin/norepinephrine reuptake inhibition (duloxetine, mirtazapine, tricyclic antidepressants, venlafaxine), norepinephrine/dopamine reuptake inhibition (bupropion), serotonin-2 antagonist/reuptake inhibition (nefazodone, trazodone), St. John´s Wort (Hypericum Perforatum), maintenance on pharmacotherapy, continuation duration, withdrawal syndrome (paroxetine/Paxil), medication adherence, managing sexual side effects of pharmacologic agents, pregnancy and pharmacologic agents, breast feeding and pharmacologic agents, pharmacotherapy not included above; interpersonal psychotherapy, cognitive behavioral therapy, short-term or focal psychodynamic psychotherapy, marital therapy, psychotherapy, not included above; other treatment not included above; ongoing clinical assessment; medical comorbidity, alcohol abuse, panic (including generalized anxiety disorder or phobia), obsessive compulsive disorder, eating disorders and anorexia nervosa, partner violence, sexual assault, pregnancy (not included above), postpartum (not included above); and depression not included above.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented

with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Consideration of benefits, harms, costs, and patient preferences

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Pharmaceutical cost data were reviewed (see Table 5 in the original guideline document).

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

University of Michigan Health System (UMHS) guidelines are reviewed by leadership and in clinical conferences of departments to which the content is most relevant. This guideline concerning depression was reviewed by members of the following departments: Family Medicine; General Medicine; Obstetrics and Gynecology; and Psychiatry.

Guidelines are approved by the Executive Committee of Clinical Affairs (ECCA).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): The following key points summarize the content of the guideline. Refer to the original guideline document for additional information. The levels of evidence [A-D] are defined at the end of the "Major Recommendations" field.

Diagnosis

Depressed patients frequently present with somatic complaints to their primary care doctor rather than complaining of depressed mood [C].

Treatment

Mild depression can be effectively treated with either medication or psychotherapy. Moderate to severe depression may require an approach combining medication and psychotherapy [A].

- Drug treatment. Fifty to sixty-five percent (50-65%) of patients respond to the first antidepressant [A]. No particular antidepressant agent is superior to another in efficacy or time to response. Choice can be guided by matching patients' symptoms to side effect profile, presence of medical and psychiatric comorbidity, and prior response [A]. Relative costs can also be considered (e.g., generics). University of Michigan Health System (UMHS) preferred agents are Fluoxetine (generic) and citalopram (Celexa®). Patients treated with antidepressants should be closely observed for possible worsening of depression or suicidality, especially at the beginning of therapy or when the dose increases or decreases [C].
- Frequent initial visits. Patients require frequent visits early in treatment to assess response to intervention, suicidal ideation, side effects, and psychosocial support systems [D].
- Continuation therapy. Continuation therapy (9-12 months after acute symptoms resolve) decreases the incidence of relapse of major depression [A]. Long term maintenance or life-time drug therapy should be considered

for selected patients based on their history of relapse and other clinical features [B].
- Education/support. Patient education and support are essential. Social stigma and patient resistance to the diagnosis of depression continue to be a problem [D].

Definitions:

Levels of Evidence

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for an overview of treatment for depression.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

Conclusions were based on prospective randomized clinical trials (RCTs) if available, to the exclusion of other data; if RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Timely recognition and accurate diagnosis of depression
- Appropriate treatment of depression, with accompanying improvement in patient mood and functioning
- Appropriate continuation and maintenance therapy to decrease the incidence of relapse of major depression
- Cost-effective prescription of antidepressant medications

Subgroups Most Likely to Benefit

Table 5 in the original guideline document includes patient profiles most likely to benefit from specific drugs.

POTENTIAL HARMS

Side effects associated with pharmacotherapy: insomnia, akathisia (a syndrome characterized by muscle restlessness), weight gain and sexual dysfunction.

- Citalopram: may be initially sedating or initially increase alertness; mild initial sedation is dose-dependent; sexual dysfunction common
- Escitalopram: sexual dysfunction common
- Fluoxetine: tends to produce more initial nervousness and arousal than other selective serotonin reuptake inhibitors (SSRIs); sexual dysfunction common
- Paroxetine: tends to cause fewer arousal and insomnia effects common with SSRIs; possesses some anticholinergic effects; sexual dysfunction common
- Sertraline: tends to increase alertness; sexual dysfunction common
- Nefazodone: BLACK BOX WARNING: Liver damage and/or liver failure in 1/250,000 patients; fatigue and dizziness; sexual dysfunction unlikely.
- Venlafaxine: side effects common to all SSRIs with more nausea; sustained hypertension risk; blood pressure increases are dose-dependent; constipation; sexual dysfunction less common.
- Duloxetine: similar to SSRIs and venlafaxine; nausea and constipation most troublesome, but, unlike venlafaxine, does not appear to produce sustained hypertension; sexual dysfunction less common.
- Mirtazapine: produces sleep; lower doses produce more sleep than do higher doses; weight gain; sexual dysfunction unlikely.
- Bupropion: most activating antidepressant available; sexual dysfunction rare.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Do not combine any of the listed antidepressants with monoamine oxidase inhibitors (MAOIs).
- Duloxetine is not to be prescribed ordinarily if concurrent heavy alcohol use and/or evidence of chronic liver disease.
- Do not use bupropion (Wellbutrin) if history of seizure, head trauma, substance abuse, bulimia, anorexia or electrolyte disturbance.
- Marital therapy should only be considered if violence is screened for and absent in the relationship.
- See Table 5 in the original guideline document for selected important drug-drug interactions.

QUALIFYING STATEMENTS

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

University of Michigan Health System. Depression. Ann Arbor (MI): University of Michigan Health System; 2005 Oct. 20 p. [3 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 Jun (revised 2005 Oct)

GUIDELINE DEVELOPER(S)

University of Michigan Health System - Academic Institution

SOURCE(S) OF FUNDING

Internal funding for University of Michigan Health System (UMHS) guidelines is provided by the Office of Clinical Affairs. No external funds are used.

GUIDELINE COMMITTEE

Depression Guideline Team

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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Guidelines Oversight Team: Connie J. Standiford, MD; Lee A. Green, MD, MPH; R. Van Harrison, PhD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information

Team Member; Relationship; Company

Thomas Schwenk, MD (none)
Linda Terrell, MD (none)
Van Harrison, PhD (none)
Elizabeth Shadigian, MD (none)
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GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: University of Michigan Health System. Depression. Ann Arbor (MI): University of Michigan Health System; 2004 May. 21 p.

GUIDELINE AVAILABILITY

Electronic copies: Available for download in Portable Document Format (PDF) from the University of Michigan Health System Web site.

AVAILABILITY OF COMPANION DOCUMENTS

- Continuing Medical Education (CME) information is available from the University of Michigan Health System Web site.
- Additionally, the original guideline document includes a Quick Screen for Depression and the Patient Health Questionnaire (PHQ-9)

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 20, 1999. The information was verified by the guideline developer on June 17, 1999. This NGC summary was updated by ECRI on October 12, 2004. The updated information was verified by the guideline developer on October 22, 2004. This summary was updated by ECRI on August 15, 2005, following the U.S. Food and Drug Administration advisory on antidepressant medications. This summary was updated by ECRI on October 3, 2005, following the U.S. Food and Drug Administration advisory on Paxil (paroxetine). This summary was updated by ECRI on October 20, 2005, following the U.S. Food and Drug Administration advisory on Cymbalta (duloxetine hydrochloride). This NGC summary was updated by ECRI on December 16, 2005. This summary was updated by ECRI on May 31, 2006 following the U.S. Food and Drug Administration advisory on Paxil (paroxetine hydrochloride).

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